

Radiolabeling and In Vivo Imaging of Transplanted Renal Lineages Differentiated from Human Embryonic Stem Cells in Fetal Rhesus Monkeys.

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Public Summary:

These studies focused on new techniques for radiolabeling cells differentiated from human embryonic stem cells for in vivo imaging, and the transplant of these cells into the kidneys of a translational model of human development and disease. The results of these studies have shown that effective methods can be developed for safely labeling the cells without altering their differentiation and proliferation capabilities, and that the cells can be found in the kidney after transplantation using in vivo imaging techniques such as positron emission tomography (PET).

Scientific Abstract:

PURPOSE: The goals of this study were to optimize radiolabeling of renal lineages differentiated from human embryonic stem (hES) cells and use noninvasive imaging (positron emission tomography (PET) and bioluminescence imaging (BLI)) to detect the cells in fetal monkeys post-transplant. **PROCEDURES:** hES cells expressing firefly luciferase (5×10^6) were radiolabeled with the optimized concentration of 10 $\mu\text{Ci}/\text{ml}$ $(64)\text{Cu-PTSM}$ then transplanted under ultrasound guidance into early second trimester fetal monkey kidneys. Fetuses were imaged in utero with PET and tissues collected for analysis 3 days post-transplant. Fetal kidneys were imaged ex vivo (PET and BLI) post-tissue harvest, and serial kidney sections were assessed by PCR for human-specific DNA sequences, fluorescent in situ hybridization (FISH) for human-specific centromere probes, and immunohistochemistry (IHC) to assess engrafted cells. **RESULTS:** Transplanted cells were readily imaged in vivo and identified at the site of injection; tissue analyses confirmed the imaging findings. Using a semi-quantitative method, one in approximately 650 cells in the kidney was shown to be of human origin by PCR and FISH. **CONCLUSIONS:** These studies suggest that hES cells differentiated toward renal lineages can be effectively radiolabeled, transplanted into fetal monkey kidneys under ultrasound guidance, monitored with PET post-transplant, and identified by PET, BLI, PCR, FISH, and IHC post-tissue harvest.

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